

List of methods for biomarkers of tobacco smoke exposure established in the Analytisch-biologisches Forschungslabor (ABF) Muenchen

(Status: May 2001)

Biomarker	Matrix	Related smoke constituent	Method	Related publication of ABF
Cotinine, nicotine	Plasma, saliva, urine	Nicotine	GC-NPD (nitrogen-selective detector)	[1]
Nicotine, cotinine, trans-3'-hydroxycotinine	Plasma, saliva	Nicotine	LC-MS/MS	-
Nicotine, cotinine, trans-3'-hydroxycotinine (+ their glucuronides), nicotine-N'-oxide, cotinine-N-oxide, norcotinine	Urine	Nicotine	LC-MS/MS <i>glucuronide werden in einem Gang mitgemessen</i>	[2] <i>in Press - Publication to come</i>
NNAL and NNAL-glucuronide	Urine	NNK	GC-TEA (thermal energy analyzer); LC-MS/MS	[3-5] <i>mit Spaltung</i>
HPB hemoglobin adducts	Blood / hemoglobin	NNK, NNN	GC-MS (NICI)	[6,7]
1,4-Butadiene	Exhaled air	1,4-Butadiene	GC-MS	-
Benzene (and other volatile aromatic compounds)	Exhaled air	Benzene etc.	GC-MS	[8]
Trans,trans-muconic acid	Urine	Benzene	GC-MS	[9-11]
Phenylmercapturic acid	Urine	Benzene	GC-MS or LC-MS/MS	[12]
Benzo[a]pyrene (BaP) hemoglobin and albumin adducts	Blood / hemoglobin, albumin	BaP	GC-MS (NICI)	[13-15]
1-Hydroxypyrene	Urine	Pyrene	HPLC-Fluorescence	[15]
4-Aminobiphenyl (4-ABP) hemoglobin and albumin adducts (and other aromatic amines)	Blood / hemoglobin, albumin	4-ABP etc	GC-MS (NICI)	[7,16]
3-Hydroxypropyl mercapturic acid	Urine	Acrolein	LC-MS/MS	[17,18]
Alkylvaline-hemoglobin adducts: methyl-, ethyl-, hydroxyethyl-, <u>cyanoethyl</u> -valine adducts	Blood / hemoglobin	Alkylating agents, acrylonitril etc.	GC-MS	[19]

PM3001172703

Glutathione detox

Malondialdehyde (MDA)	Urine	(Oxidative stress, lipidperoxidation)	HPLC-UV	-
8-Hydroxy-2'-deoxyguanosine (8-OHdG)	Cellular DNA (e.g. lymphocytes)	(Oxidative stress, DNA oxidation)	HPLC-ECD	[20]
8-Hydroxy-2'-deoxyguanosine (8-OHdG)	Urine	(Oxidative stress, DNA oxidation)	LC-MS/MS <i>= metabolite</i>	[21]
Mutagenic activity	Urine	Mutagens	Ames test (with strains TA98, YG1024)	[22,23]
Thioethers	Urine	Electrophilic compounds	Photometry	[23]
Genotypes of CYP1A1, CYP2A6, CYP2E1, CYP1B1, NAT1, NAT2, GSTM1, GSTT1, GSTP1	Blood cells	(Modifier of biomarker levels)	PCR (\pm restriction enzyme analyse)	[24,25]

References

- [1] Scherer G, Meger-Kossien I (2000) Cotinin. In: Greim H (ed) Deutsche Forschungsgemeinschaft (DFG): Analysen in biologischem Material, vol Band 2. Wiley-VCH Verlag GmbH, Weinheim
- [2] Meger M, Meger-Kossien I, Schuler-Metz A, Janket D, Scherer G (2001) Simultaneous determination of nicotine and eight nicotine metabolites in urine of smokers using liquid chromatography tandem mass spectrometric (LC-MSMS) detection. J Chromatogr B (submitted)
- [3] Meger M, Meger-Kossien I, Dietrich M, Tricker AR, Scherer G, Adlkofer F (1996) Metabolites of 4-(N-methylnitrosamino)-1-(3-pyridyl)-1-butanone in urine of smokers. European Journal of Cancer Prevention 5 (Supp. 1):121-124
- [4] Meger M, Meger-Kossien I, Scherer G (1998) Metabolites of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) in urine of smokers and nonsmokers. Proceedings of the American Association for Cancer Research, Vol. 39, March 1998.
- [5] Meger M, Meger-Kossien I, Riedel K, Scherer G (2000) Biomonitoring of environmental tobacco smoke (ETS)-related exposure to 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK). Biomarkers 5:33-45
- [6] Richter E, Branner B, Kutzer C, Donh rl AME, Scherer G, Tricker AR, Heller W-D (1995) Comparison of biomarkers for exposure to environmental tobacco smoke: Cotinine and haemoglobin adducts from aromatic amines and tobacco-specific nitrosamines in pregnant smoking and nonsmoking women. In: Maroni M (ed) healthy buildings '95 an international conference on healthy buildings in mild climate. healthy buildings '95, Milano
- [7] Branner B, Kutzer C, Zwickenkflug W, Scherer G, Heller W-D, Richter E (1998) Haemoglobin adducts from aromatic amines and tobacco-specific nitrosamines in pregnant smoking and nonsmoking women. Biomarkers 3:35-47
- [8] Riedel K, Ruppert T, Conze C, Scherer G, Adlkofer F (1996) Determination of benzene and alkylated benzenes in ambient and exhaled air by microwave desorption coupled with gas chromatography-mass spectrometry. J Chromatogr 719:383-389

- [9] Ruppert T, Scherer G, Tricker AR, Rauscher D, Adlkofer F (1995) Determination of urinary *trans,trans*-muconic acid by gas chromatography-mass spectrometry. *J Chromatogr* 666:71-76
- [10] Ruppert T, Scherer G, Tricker AR, Adlkofer F (1997) *trans, trans*-muconic acid as a biomarker of non-occupational environmental exposure to benzene. *Int Arch Occup Environ Health* 69:247-251
- [11] Scherer G, Renner T, Meger M (1998) Analysis and evaluation of *trans,trans*-muconic acid as a biomarker for benzene exposure. *J Chromatogr* 717:179-199
- [12] Scherer G, Meger M, Meger-Kossien I, Pachinger A (2001) Biological monitoring of the tobacco smoke-related exposure to benzene. *Proc American Assoc Cancer Res* 42:150
- [13] Frank S, Renner T, Ruppert T, Scherer G (1998) Determination of albumin adducts of (+)-*anti*-benzo[a]pyrene-diol-epoxide using an high-performance liquid chromatographic column switching technique for sample preparation and gas chromatography-mass spectrometry for the final detection. *J Chromatogr* 713:331-337
- [14] Frank S, Renner T, Ruppert T, Scherer G (1999) Determination of albumin adducts of (+)-*anti*-benzo[a]pyrene-diol-epoxide an HPLC column switching technique for sample preparation and GC-NCI-MS for the final detection. *Polycyclic Aromatic Compounds* 17:135-144
- [15] Scherer G, Frank S, Riedel K, Meger-Kossien I, Renner T (2000) Biomonitoring of exposure to polycyclic aromatic hydrocarbons of nonoccupationally exposed persons. *Cancer Epidemiol Biomarkers & Prev* 9:373-380
- [16] Richter E, Rösler S, Scherer G, Gröbl A, Krämer U, Behrendt H (2001) Haemoglobin adducts from aromatic amines in children are influenced by regional differences but not by exposure to environmental tobacco smoke. *Int Arch Occup Environm Health* (in press)
- [17] Scherer G, Krause G, Mascher D, Schmid E (2000) Biological monitoring of the tobacco smoke-related exposure to acrolein. *Proceedings of the American Association for Cancer Research*. 91st Annual meeting, April 1-5, 2000, San Francisco.
- [18] Mascher DG, Mascher HJ, Scherer G, Schmid ER (2001) High-performance liquid chromatographic-tandem mass spectrometric determination of 3-hydroxypropylmercapturic acid in human urine. *J Chromatogr B* 750:163-169
- [19] Scherer G, Urban M, Meger M (2001) Biological monitoring of the tobacco smoke-related exposure to alkylating agents. *Proc American Assoc Cancer Res* 42:149-150
- [20] Daube H, Scherer G, Riedel K, Ruppert T, Tricker AR, Rosenbaum P, Adlkofer F (1997) DNA adducts in human placenta in relation to tobacco smoke exposure and plasma antioxidant status. *J Cancer Res Clin Oncol* 123:141-151
- [21] Renner T, Fechner T, Scherer G (2000) Fast quantification of the urinary marker of oxidative stress 8-hydroxy-2'-deoxyguanosine using solid-phase extraction and high-performance liquid chromatography with triple-stage quadrupole mass detection. *J Chromatogr B* 738:311-317
- [22] Scherer G, Westphal K, Adlkofer F, Sorsa M (1989) Biomonitoring of exposure to potentially mutagenic substances from environmental tobacco smoke. *Environ Int* 15:49-56
- [23] Scherer G, Doolittle DJ, Ruppert T, Meger-Kossien I, Riedel K, Tricker AR, Adlkofer F (1996) Urinary mutagenicity and thioethers in nonsmokers: Role of environmental tobacco smoke (ETS) and diet. *Mutat Res* 368:195-204
- [24] Krause G, Garganta F, Kosytorz P, Scherer G (1998) Genotyping metabolic polymorphisms in a cohort of Caucasians and SSCP-analysis of point mutations in human *hprt* exons 7 and 8. *Electrophoresis* 19:2380-2388
- [25] Paschke T, Garganta F, Wolz L, Scherer G (2000) Development of a simple and specific CYP2A6 genotyping method. *Proceedings of the American Association for Cancer Research*. 91st annual meeting, April 1-5, 2000, San Francisco.